PATENT COOPERATION TREATY

From the INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

11 Oct -04

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26/8/04

PU0284-PCT

PCT

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 66)

To:

Amersham Biosciences AB
Björkgatan 30
451 84 Uppsala

RECEIVED
2004 -08- 16
U-A PD

Date of mailing (day/month/year) 12 -08- 2004

Applicant's or agent's file reference
PU0284-SE

REPLY DUE within 60 months/days from the above date of mailing

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/SE 2003/001435	12.09.2003	31.10.2002

International Patent Classification (IPC) or both national classification and IPC
C07K 16/18, G06T 17/00, G01N 33/563

Applicant
Amersham Biosciences AB et al

1. ☐ The written opinion established by the International Searching Authority:
   ☐ is ☐ is not
   considered to be a written opinion of the International Preliminary Examining Authority.

2. This first (first, etc.) opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 31.02.2005

Name and mailing address of the IPEA/SE	Authorized officer
Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 46 8 667 72 88	Ida Christensen/BS Telephone No. 46 8 782 25 00

Form PCT/IPEA/408 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this opinion has been established on the basis of *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed.")*:

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages _____ as amended (together with any statement) under Article 19
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages _____ received by this Authority on _____
pages _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-3 (partially), 25

because:

☒ the said international application, or the said claims Nos. 25 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

Claim 25 relates to a machine readable data storage medium, which is considered to be a mere presentation of information (PCT Rule 67.1(v)).

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 1-3 (part.) are so unclear that no meaningful opinion could be formed *(specify)*:

Present claims 1-3 relate to a compound containing a binding pocket. The compound is not considered to be sufficiently defined. It is even uncertain whether the binding pocket is sufficiently defined by the structure coordinates in order to be reproducibly generated (see also box VIII).
Claims 1-3 relate to an extremely large number of possible compounds.

.../.../...

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-3 (partially), 25

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box III.2

Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful examination over the whole of the claimed scope is impossible.
Consequently, the examination has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts related to a compound consisting of the IgG kappa constant region (either the light chain alone or in combination with the heavy chain).

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Box No. V **Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-3 (NO)
	Claims	
Inventive step (IS)	Claims	1-24 (NO)
	Claims	
Industrial applicability (IA)	Claims	
	Claims	

2. Citations and explanations:

Reference will be made to the following relevant documents cited in the International Search Report:

D1) The Journal of Biological Chemistry, 271(21):12191-12198 (1996), Chacko S & Padlan E A.
D2) Pathology International, 51(4):264-270 (2001), Hoshii Y et al.

D1 discloses the 3D-structure of the Fab fragment from TR1.9, which is a human IgG1-kappa autoantibody (see the abstract).

D2 describes synthetic peptides corresponding to positions 116-133 of a human Ig-kappa light chain constant region and polyclonal antibodies against said peptides for the detection of disease (the abstract).

The present application relates to the identification of a novel binding site, which is located in a strictly conserved region located between a light chain and a heavy chain of a human IgG kappa antibody. The aim is to identify compounds which are capable of binding specifically to said binding site and thereby may be used as affinity ligands in affinity chromatography for the purification of IgGs.

The subject-matter of claims 1-3 is not restricted to the newly identified binding site. Instead, claims 1-3 also relate to previously known compounds, such as the Fab fragment disclosed in D1, and therefore claims 1-3 lack novelty.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: box V

The polypeptide according to claims 4-8, the complex according to claims 9-11 and the computer according to claims 23-24 are novel.

However, it is previously known to isolate the constant region from an IgG-kappa Fab fragment and D2 describes peptides corresponding to parts of the constant region. It is therefore considered obvious to a person skilled in the art to isolate a polypeptide according to claims 4-8. The structure coordinates which are described in claims 7-8 do not lead to a different product.

The isolated and purified polypeptide according to claims 4-8 (consisting of a limited portion of a human IgG light and/or heavy chain) has not been produced and used in the present application. Instead, an entire IgG-kappa Fab fragment has been used in the experiments for identifying ligands. But even if such a polypeptide were to be produced, it would not be considered to involve an inventive step.

The complex according to claims 9-11 and the computer according to claims 23-24 are not considered to confer any further inventive features *per se*.

Therefore, it is considered that an inventive step is lacking for the subject-matter of claims 4-11 and 23-24.

The method of claims 12-18 and the use according to claims 19-22 are novel.

It is doubted that the method or the use would function if a polypeptide consisting of a portion of the light chain only or a portion of the heavy chain only would be used.

.../.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: box V

Consequently, with the present reference to claims 4-5, the subject-matter of claims 12-22 is not considered to involve an inventive step.

It is considered that the method and the use would work if (parts of) the constant regions of the light and of the heavy chain are used together. The region containing the relevant binding pocket should be clearly described in the claims, in order to exclude the two clefts which were also identified by the present inventors but not further investigated, or other possible binding pockets yet to be identified in the constant region.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-3 relate to a compound containing a binding pocket. The compound is not considered to be sufficiently defined. It is even uncertain whether the binding pocket is sufficiently defined by the structure coordinates in order to be reproducibly generated (see also box III).